Anthrax

Signs and Symptoms	Symptoms depend on the type of infection; all types can cause severe illness: • **Cutaneous:** painless, pruritic papules or vesicles which form black eschars, often surrounded by edema or erythema. Fever and lymphadenopathy may occur. • **Ingestion:** Oropharyngeal: mucosal lesion in the oral cavity or oropharynx, sore throat, difficulty swallowing, and swelling of neck. Fever, fatigue, shortness of breath, abdominal pain, nausea/vomiting may occur. Gastrointestinal: abdominal pain, nausea, vomiting/diarrhea, abdominal swelling. Fever, fatigue, and headache are common. • **Inhalation:** Biphasic, presenting with fever, chills, fatigue, followed by cough, chest pain, shortness of breath, nausea/vomiting, abdominal pain, headache, diaphoresis, and altered mental status. Pleural effusion or mediastinal widening on imaging. • **Injection:** Severe soft tissue infection; no apparent eschar. Fever, shortness of breath, nausea may occur. Occasional meningeal or abdominal involvement.		
Incubation	Usually < 1 week but as long as 60 days for inhalational anthrax		
Case classification	**Clinical criteria**: An illness with at least one specific OR two non-specific symptoms and signs that are compatible with one of the above 4 types, systemic involvement, or anthrax meningitis; OR death of unknown cause and consistent organ involvement		
	Confirmed: Clinically consistent with isolation, positive IHC, 4-fold rise in antibodies, PCR, or LF MS	**Probable:** Clinically consistent with consistent Gram-positive rods, OR positive test from CLIA-accredited laboratory, OR epi evidence relating to anthrax	**Suspect:** Clinically consistent with anthrax test ordered but no epi evidence
Differential diagnosis	Varies by form; mononucleosis, cat-scratch fever, tularemia, plague, sepsis, bacterial or viral pneumonia, mycobacterial infection, influenza, hantavirus		
Treatment	Appropriate antibiotics and supportive care; anthrax antitoxin if spores are activated. A vaccine is available for persons at occupational risk.		
Duration	Varies by form; person-to-person spread is rare		
Exposure	Contact with infected animals or animal products such as wool, hides, or hair, contact with infected animal carcasses or eating contaminated meat.		
Laboratory testing	LHJ and CDE arrange testing for individual cases or confirm isolates • Washington State Public Health Laboratories can culture or confirm isolates • **Best specimens**: isolate in screw-top slant; swab of eschar; aspirate fluid, stool, CSF, tissue kept moist *Specimen shipping (Section 4):* • Keep isolate at **room** temperature, other specimens cold, ship with Bioterrorism form https://doh.wa.gov/sites/default/files/legacy/Documents/5230/302-018-BioterrorismSpecimen.pdf		
Public health actions **URGENT**	Immediately report to CDE any suspected or laboratory positive cases • Identify risk exposure: contact with animals or animal products, work with animals or in microbiology laboratory • Identify close contacts or others potentially exposed (household, hospital, lab) and evaluate, if symptomatic arrange testing, if asymptomatic educate about symptoms and arrange post-exposure antibiotic prophylaxis and monitoring for symptoms • Consider environmental evaluation *Infection Control:* standard precautions; contact precautions for draining lesions/wounds		

Anthrax

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To rapidly detect anthrax-related illness and promptly treat those who are ill.
2. To promptly identify the source of infection, including identification of intentional release of anthrax in context of a bioterrorist attack.
3. To involve appropriate public safety agencies in an investigation.
4. To rapidly implement control measures.

B. Legal Reporting Requirements

1. **Health care providers and Health care facilities**: *immediately* notifiable to **local health jurisdiction**
2. **Laboratories: any** *Bacillus anthracis and Bacillus cereus biovar anthracis only immediately* notifiable to **local health jurisdiction**; submission required – presumptive positive *B. anthracis* isolate (2 business days). Any other specimens with results indicating *B. anthracis* infection should also be submitted (see Sections 3 and 4)
3. **Veterinarians**: animal cases notifiable to Washington State Department of Agriculture http://app.leg.wa.gov/WAC/default.aspx?cite=16-70
4. **Local health jurisdictions**: *immediately* notifiable to Washington State Department of Health (DOH) Office of Communicable Disease Epidemiology (CDE).

C. Local Health Jurisdiction Investigation Responsibilities

1. **All cases or potential cases must be immediately reported to DOH: 1-877-539-4344 or 206-418-5500.** Conduct a rapid assessment to determine whether bioterrorism is a potential. **If bioterrorism is suspected, immediately notify DOH of this possibility**
2. Facilitate the transport of specimens to the Washington State Public Health Laboratories.
3. Determine the source of infection.
4. Identify other persons exposed and recommend chemoprophylaxis as indicated.
5. Report all confirmed, probable, and suspect cases to CDE. Complete the case report form www.doh.wa.gov/Portals/1/Documents/5100/210-055-ReportForm-Anthrax.pdf and enter the data into the Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Bacillus anthracis is an aerobic, non-motile, spore-forming, encapsulated, gram-positive, rod-shaped bacterium. *B. cereus*, biovar *anthracis*, can also express anthrax toxins. It is not a suspected case of anthrax if a laboratory requests confirmatory testing to distinguish *B. anthracis* from *B. megaterium* or other species when anthrax is not a likely diagnosis.

B. Description of Illness

Anthrax causes several main clinical syndromes, depending on the route of exposure.

1. Cutaneous anthrax (>95% of human anthrax cases)

Cutaneous disease is characterized by one or more painless, itchy papules or vesicles on the skin, typically on exposed skin areas such as the face, neck, forearms, or hands. Within 7–10 days of the initial lesion, a papule lesion forms a skin ulcer. The ulcer subsequently crusts over, forming a painless black eschar that is the hallmark of cutaneous anthrax. In addition, localized swelling, painful swollen regional lymph nodes, and systemic symptoms can occur. The untreated case fatality rate is 5–20%; death is rare with appropriate therapy.

2. Ingestion anthrax

Ingestion anthrax is an uncommon form of the disease. It can present as two sub-types:

Oropharyngeal: When anthrax spores germinate in the oropharynx, a mucosal lesion may be observed in the oral cavity or oropharynx. Symptoms include sore throat, difficulty swallowing, and swelling of the neck. Symptoms resembling a viral respiratory illness may occur, as well as cervical lymphadenopathy, ascites, and altered mental status. Case fatality was 50% in an oropharyngeal outbreak in Thailand due to contaminated water buffalo meat.

Gastrointestinal: When anthrax spores germinate in the lower gastrointestinal tract, symptoms include abdominal pain, nausea, vomiting or diarrhea (either of which may contain blood), and abdominal swelling. Less specific symptoms such as fever, fatigue, and headache are also common. Altered mental status and ascites may be observed. The case fatality rate is estimated to be 25–60%. While antibiotic treatment may decrease deaths, the nonspecific initial presentation makes diagnosis difficult in the absence of a known exposure or cluster of disease. Recent gastrointestinal outbreaks due to contaminated meat have occurred in Bangladesh, Kenya, the Philippines, and Uganda.

3. Inhalation anthrax

Inhalational anthrax typically progresses through two distinct stages. The first, lasting from several hours to several days, involves influenza-like symptoms such as low grade fever, non-productive cough, malaise, fatigue and chest discomfort. The second stage has abrupt onset of high fever, severe respiratory distress (dyspnea and hypoxia), and shock. Non-thoracic symptoms such as nausea, vomiting, abdominal pain, headache, sweating, and altered mental status may occur. Imaging often shows a widened mediastinum. Therapy must be started early in the course of illness to be effective. Of 11 people who developed inhalational disease during the 2001 anthrax attacks, five (45%) died.

4. Injection anthrax

Injection anthrax generally presents as a severe soft tissue infection manifested as significant edema or bruising after a contaminated injection. No eschar is apparent. Nonspecific symptoms such as fever, shortness of breath, or nausea are sometimes the first indication of illness. Occasionally patients present with meningeal or abdominal involvement. Injection anthrax has been reported in northern Europe among people injecting heroin.

5. Meningeal anthrax

Meningeal anthrax may complicate any form of anthrax, and may also be a primary manifestation. The rarest form of anthrax, it occurs as an acute illness with fever, headache, nausea, vomiting, and fatigue. Meningeal signs, altered mental status, and other neurological signs such as seizures or focal signs are usually present. Most patients with anthrax meningitis have CSF abnormalities consistent with bacterial meningitis, and the CSF is often described as hemorrhagic. Mortality is likely 100% even with treatment.

C. Anthrax in Washington

The last documented human case of anthrax in Washington occurred in 1957.

In 2001, processed *B. anthracis* spores put in letters caused an outbreak of 22 anthrax cases in the eastern United States. In 2009, a woman in New Hampshire developed gastrointestinal anthrax after attending a drumming event using drums with imported animal hides Gastrointestinal Anthrax after an Animal-Hide Drumming Event - 2009 (cdc.gov). Minnesota identified a case of inhalational anthrax in 2011 in a man who had traveled through several states and had multiple exposures to animals, animal products, and dust in areas with wildlife; however, no specific source was identified following a thorough multi-state and multi-agency investigation Emerg Infect Dis 2014 Feb. Animal cases are periodically identified in cattle and other herd animals including infected bison in Saskatchewan and North Dakota during 2015 and a Texas outbreak in 2019 affecting animals and one human Emerg Infect Dis 2020 Dec.

For CDC publications including diagnosis, prophylaxis, and guidelines, see: https://www.cdc.gov/anthrax/resources/anthrax-mmwrs.html and https://www.cdc.gov/anthrax/index.html

D. Reservoir

Historically, exposure to anthrax has resulted from contact with herbivores (such as cattle, sheep, or goats) that are ill with the disease or from contaminated products (such as meat, wool, hides or hair) from ill herbivores. While dormant anthrax spores are found in the soil of many parts of the world including parts of the United States, infection resulting from direct inhalation of natural spores in soil is felt to be very rare.

From a bioterrorism perspective, the main concern is the intentional processing of anthrax spores to produce a higher potential for causing infection, particularly inhalational anthrax. The extent of stockpiling of such biological weapons by nations and/or terrorist groups is unknown.

E. Modes of Transmission

Transmission can occur from skin contact with contaminated animals or animal products (e.g., wool or hides), eating contaminated food such as meat from an infected animal, or inhaling processed spores. Imported raw hides, such as used for animal skin drums, have been contaminated with spores and have caused illness in the United States.

F. Incubation period

The incubation period is usually < 1 week but as long as 60 days for inhalation anthrax, 1–12 days for cutaneous anthrax, and 1–7 days for ingestion anthrax.

G. Period of Communicability

Person-to-person spread is rare, and has only been documented with the cutaneous form.

H. Treatment

Prompt administration of appropriate antibiotics is essential for effective treatment. Note that there may be resistance to extended-spectrum cephalosporins or to trimethoprim/sulfamethoxazole. For specific information regarding the treatment of anthrax http://www.cdc.gov/anthrax/medicalcare/treatment/index.html.

3. CASE DEFINITIONS

A. Clinical description

- **Cutaneous anthrax:** Usually begins as a small, painless, pruritic papule on an exposed surface, which progresses through a vesicular stage into a depressed black eschar; the eschar is often surrounded by edema or erythema and may be accompanied by lymphadenopathy. Fever is also common.
- **Ingestion anthrax** presents as two sub-types:
  Oropharyngeal: When anthrax spores germinate in the oropharynx, a mucosal lesion may be observed in the oral cavity or oropharynx. Symptoms include sore throat, difficulty swallowing, and swelling of the neck. Less specific symptoms include fever, fatigue, shortness of breath, abdominal pain, and nausea/vomiting; the symptoms may resemble a viral respiratory illness. Cervical lymphadenopathy, ascites, and altered mental status may be observed.

  Gastrointestinal: When anthrax spores germinate in the lower gastrointestinal tract, symptoms include abdominal pain, nausea, vomiting or diarrhea (either of which may contain blood), and abdominal swelling. Less specific symptoms such as fever, fatigue, and headache are also common. Cervical lymphadenopathy, ascites, and altered mental status may be observed.
- **Inhalation anthrax:** Often described as a biphasic illness. Early nonspecific symptoms of inhalation anthrax include fever and fatigue. Localized thoracic symptoms such as cough, chest pain, and shortness of breath follow, as may non-thoracic symptoms such as nausea, vomiting, abdominal pain, headache, diaphoresis, and altered mental status. Lung sounds are often abnormal and imaging often shows pleural effusion or mediastinal widening.
- **Injection anthrax**: Usually presents as a severe soft tissue infection manifested as significant edema or bruising after an injection. No eschar is apparent, and pain is often not described. Nonspecific symptoms such as fever, shortness of breath, or nausea are sometimes the first indication of illness. Occasionally patients present with meningeal or abdominal involvement. A coagulopathy is not unusual.
- Additional considerations:
  1. Signs of systemic involvement from the dissemination of either the bacteria and / or its toxins can occur with all types of anthrax and include fever or hypothermia, tachycardia, tachypnea, hypotension, and leukocytosis. One or more of these signs are usually present in patients with ingestion anthrax, inhalation anthrax, and

injection anthrax, and may be present in up to a third of patients with cutaneous anthrax.

2. Anthrax meningitis may complicate any form of anthrax, and may also be a primary manifestation of infection. Initial symptoms include fever, headache (which is often described as severe), nausea, vomiting, and fatigue. Meningeal signs (e.g., meningismus), altered mental status, and other neurological signs such as seizures or focal signs are usually present. Most patients with anthrax meningitis have cerebral spinal fluid (CSF) abnormalities consistent with bacterial meningitis, and the CSF is often described as hemorrhagic.

Clinical criteria: An illness with at least one specific OR two non-specific symptoms and signs that are compatible with cutaneous, ingestion, inhalation, or injection anthrax; systemic involvement; or anthrax meningitis; OR a death of unknown cause and organ involvement consistent with anthrax.

B. Laboratory criteria for diagnosis

Presumptive laboratory criteria

1. Gram stain demonstrating Gram-positive rods, square-ended, in pairs or short chains
2. Positive result on a test with established performance in a CLIA-accredited laboratory

Definitive laboratory criteria

1. Culture and identification of *Bacillus anthracis* from clinical specimens by the Laboratory Response Network (LRN); **OR**
2. Demonstration of *B. anthracis* antigens in tissues by immunohistochemical staining using both *B. anthracis* cell wall and capsule monoclonal antibodies; **OR**
3. Evidence of a four-fold rise in antibodies to protective antigen between acute and convalescent sera or a four-fold change in antibodies to protective antigen in paired convalescent sera using Centers for Disease Control and Prevention (CDC) quantitative anti-PA IgG ELISA testing; **OR**
4. Detection of *B. anthracis* or anthrax toxin genes by the LRN-validated polymerase chain reaction and/ or sequencing in clinical specimens collected from a normally sterile site (such as blood or CSF) or lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal); **OR**
5. Detection of lethal factor (LF) in clinical serum specimens by LF mass spectrometry

Also report identification of *Bacillus cereus*, biovar *anthracis*.

Epidemiologic evidence includes:

1. Exposure to environment, food, animal, materials, or objects that is suspect or confirmed to be contaminated with *B. anthracis;*
2. Exposure to the same environment, food, animal, materials, or objects as another person who has laboratory-confirmed anthrax;

3. Consumption of the same food as another person who has laboratory-confirmed anthrax.

C. Case classification (2018)

Suspect: A case that meets the clinical criteria AND for whom an anthrax test was ordered, but with no epidemiologic evidence relating it to anthrax.

Probable: A clinically compatible illness that does not meet the confirmed case definition, but with one of the following:

- Epidemiological evidence relating to anthrax; OR
- Presumptive but not definitive laboratory evidence.

Confirmed: A clinically compatible illness with definitive laboratory evidence.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Clinical suspicion based on symptoms or known exposures is the most critical element for accurate diagnosis. In the absence of trauma, a chest X-ray with mediastinal widening is suggestive of inhalational anthrax. A painless black eschar suggests cutaneous anthrax. Ingestion anthrax would result from consumption of contaminated food, such as during international travel. Injection anthrax generally results from injecting drugs. Meningeal anthrax is a complication of any form of the disease.

Confirmatory laboratory testing must be performed by a reference laboratory such as the Washington State Public Health Laboratories (PHL).

Laboratory tests available for the diagnosis of anthrax include gram stain and culture, electrophoretic immunotransblot (EITB) reaction, time-resolved fluorescent assay, real-time PCR, and EIA to detect IgG in acute and convalescent sera. Obtain specimens for culture before initiating antimicrobial therapy. For details of specimen requirements (searched by scientific name of agent) http://www.doh.wa.gov/ForPublicHealthandHealthcareProviders/PublicHealthLaboratories/MicrobiologyLabTestMenu

B. Tests Available at the Washington State Public Health Laboratories (PHL)

PHL will do culture and PCR. In addition, clinical laboratories can send suspect *Bacillus* cultures to PHL for species identification; such cultures are generally *B. megaterium*, another non-motile *Bacillus.* Contact PHL for shipping instructions. If *B. anthracis* has not been confirmed and is clinically unlikely, the specimen can be sent to rule out *B. anthracis* but should still be preapproved. Confirmed *B. anthracis* should not be shipped.

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

C. Specimen Collection

For information regarding specimen collection: http://www.cdc.gov/anthrax/specificgroups/lab-professionals/cdcspecimens.html.

All specimens should be submitted to PHL with a completed Bioterrorism form:
https://doh.wa.gov/sites/default/files/legacy/Documents/5230//302-018-BioterrorismSpecimenSubmission-2175.pdf

5. ROUTINE CASE INVESTIGATION

Notify Office of Communicable Disease Epidemiology (CDE) at 206-418-5500 or 877-539-4344 of any suspected case. **The FBI may want to be present for interviews even if bioterrorism is not suspected**. Immediately interview the case, suspect or confirmed, and others who may be able to provide pertinent information.

A. Evaluate the Diagnosis

Review the clinical presentation and laboratory findings. **Confirmatory laboratory testing must be performed by a reference laboratory such as the Washington State Public Health Laboratories (PHL).** Facilitate the transport of specimens (obtain before antibiotic therapy) to PHL for confirmatory testing.

B. Identify Potential Sources of Infection

Treat any case of anthrax as a potential bioterrorism incident until this can be ruled out. Any resulting investigation is potentially both a public health and a criminal investigation. Local public safety or the FBI may need to be involved during the interview or for follow-up of potential exposures. if animals in the state are a suspected source, Washington State Department of Agriculture (domestic animals) or Department of Fish and Wildlife (wildlife) may need to be involved.

Ask about potential sources of transmission in the exposure period, including:

- Contact with animals or animal products (e.g., hides, rawhide drums, bones, wool, wool blankets, etc.), including the country of origin of any such animals or products;
- Inhalation of dust from soil, grain or hay;
- Occupational exposures (e.g., agricultural worker, veterinarian, wildlife/field biologist, wool-sorter, drum-maker, etc.); or
- Attendance at a large social gathering.

C. Infection Control / Case Management

1. Hospitalized patients should be cared for using standard precautions.
2. Use contact precautions if uncontrolled drainage is occurring from a wound.

D. Identify Potentially Exposed Persons

Contacts of the case are not generally considered at risk because person to person transmission is rare. The concern for contacts of the case is whether any contacts shared the same exposure source as the case. Once the route and likely venue of the case's exposure have been established:

1. Determine the time and spatial extent of the exposure.
2. Develop a list of persons with suspected exposure based on interviews with ill persons as well as other evidence such as attendee lists or credit card receipts of any functions where exposure is suspected to have occurred.
3. Discuss interview plan with CDE to determine if FBI presence is needed at interview.

4. Contact all potentially exposed persons to assess for illness and to discuss possible prophylaxis.

E. Management of Exposed Persons

Educate persons potentially exposed to the same source as the patient about the incubation period and symptoms of anthrax, including specific symptoms that should prompt immediate medical evaluation, such as: fever, cough, shortness of breath, vomiting, diarrhea, or appearance of a painless black scar on the skin.

For information regarding post-exposure antimicrobial and vaccine prophylaxis for exposed individuals (Tables 1, 2) see: http://www.cdc.gov/mmwr/pdf/rr/rr5906.pdf.

F. Environment Measures

Consider directed environmental sampling of a suspect venue to localize the exposure after consultation with an expert in such sampling. Expert advice is also needed for decontamination of processed spores in buildings.

6. MANAGING SPECIAL SITUATIONS

A. Bioterrorist Event

Anthrax has been classified as a "category A" agent for bioterrorism; it is easy to disseminate by aerosol and can cause severe illnesses with high mortality rates. An intentional release (bioterrorist event) should be suspected if unusual clusters are seen in otherwise healthy individuals or in people in buildings with common ventilation systems. **Call Office of Communicable Disease Epidemiology immediately at 1-877-539-4344 or 206-418-5500 if anthrax is suspected.**

B. Response Following Discovery of a Suspicious Substance

1. Evaluation by Local Law Enforcement

Immediately call 911 if a suspicious substance (white powder or otherwise) is discovered. The initial key step is for law enforcement to assess whether or not a “credible threat” exists. They may call in a hazardous materials (Haz-Mat) team to assess the situation.

2. Public Health Response

If law enforcement concludes that there is a credible threat, additional laboratory tests should be performed at state or federal laboratories. Public health agencies may be involved with the ongoing investigation or prophylaxis of those exposed.

7. ROUTINE PREVENTION

A. Vaccine Recommendations

Pre-exposure vaccination is currently recommended only for the following groups:

- Persons who work directly with high concentrations of the organism in the laboratory.
- Persons handling potentially infected animals in research settings or in areas with a high incidence of enzootic anthrax or when standards and restrictions are insufficient to prevent exposure to *B. anthracis* spores.
- Persons involved in environmental investigation or remediation efforts.

- Military personnel deployed to areas with high risk for exposure to the organism.

For information regarding pre-exposure vaccination for high risk individuals, see (Tables 2, 3): http://www.cdc.gov/mmwr/pdf/rr/rr5906.pdf.

B. Prevention Recommendations

Recent cutaneous anthrax cases in the United States have been associated with untreated imported animal hides. Only processed animal hides should be used for products such as drums.

ACKNOWLEDGEMENTS

This document is a revision of the Washington State Guidelines for Notifiable Condition Reporting and Surveillance published in 2002 which were originally based on the Control of Communicable Diseases Manual (CCDM), 17th Edition; James Chin, Ed. APHA 2000. We would like to acknowledge the Oregon Department of Human Services for developing the format and select content of this document.

UPDATES

January 2010: Updated case definition with new meningeal syndrome and new suspect and probable definitions (Section 3); new link for reporting form (Section 1).

January 2011: The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision. Clarification of LHJ responsibilities if bioterrorism is suspected and the inclusion of reporting all case classifications were added to Section 1C. Updated historical case details were added to Section 2B-3 and 2C. The laboratory evidence and case definition sections were reformatted (Section 3B and 3C). Section 4A and 5A were modified to reflect that confirmatory testing should be performed at WA PHL or another PHL. Vaccine recommendations were updated.

June 2012: A description of the 2011 inhalational anthrax case in Minnesota was added in Section 2C. Information about communicable period was clarified in Section 2G. Additional discussion regarding potential sources is included in Section 5.

July 2014: Time resolved fluorescence testing is not performed at PHL and was deleted from list of available tests. The link for CDC anthrax treatment guidance was updated.

November 2015: Noted that LHJ investigations of suspect cases including interviews may need to include the FBI. New link added for PHL directory of microbiology services. Section 6 (Controlling Further Spread) incorporated into Section 5 (Routine Case Investigation) and remaining sections were renumbered.

January 2018: Added front page, updates to the description of illness consistent with the 2017 case definition, updates to the case definition

January 2022: Routine review

December 2022: For 2023 WAC revision combined provider and facility reporting requirement (Section 1B2), updated laboratory submission (Section 1B3)